Amendments to the Claims

This Listing of Claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

1. (Currently Amended): Conjugates One or more conjugate[[s]] of a polyamine[[s]] with an acidic retinoid[[s]], having pharmaceutical properties, in which [[the]] an R group in a) and/or b) below of the acyl group(s) RCO is one of the retinoid residues R¹-R⁶ set forth in the following acidic retinoids and polyene chain shortened all trans retinoic acid analogues:

and said polyamine[[s]] is [[are]]:

a linear tri, tetra and hexa- polyamine[[s]],
in which case the one or more conjugate[[s]] have has the following general formulae:

Appl. No. 10/549,905

Atty. Docket No.: 13907-02

Response to May 12, 2008 Final Office Action

wherein n is 1 to 9; or

[[d)]] b) a branched (dimeric) polyamine[[s]],

in which case the one or more conjugate[[s]] have has the following general formula:

wherein

R' is COR or $(CH_2)_3$ NHCOR and R" is COR or $(CH_2)_3$ NHCOR and n is one of the numbers 1, 2 or 7.

- 2. (Currently Amended): A method for the preparation of the one or more conjugate a compound according to claim 1 involving initially step a), followed by step b) or step c):
 - a) synthesis of a compound[[s]] with the general formula

wherein R is one of the retinoid residues R^1 - R^6 of claim 1, which involves esterification of <u>an</u> acidic retinoid[[s]] with HOSu in the presence of [[the]] <u>a</u> coupling agent DCC and purification with flash column chromatography to obtain <u>a</u> purified succinimidyl ester[[s]];

- b) direct selective acylation of the primary amino groups functions of the polyamine[[s]] with the purified succinimidyl ester[[s]]; or
- c) selective acylation of the secondary amino groups of the polyamine[[s]], protected at their its primary amino functions with a trifluoroacetyl or a 9-fluorenylmethoxycarbonyl group, with the acidic retinoid[[s]] identified in Fig. 2 of claim 1 in the presence of the coupling agent PyBrOP, followed by deprotection.

Appl. No. 10/549,905

Atty. Docket No.: 13907-02

Response to May 12, 2008 Final Office Action

3. (Currently Amended): A method according to claim 2, which method involves the direct selective acylation of the primary amino functions of the polyamine[[s]] or their its corresponding hydrochloride or trifluoroacetate salts with the compound[[s]] of the step a) of claim 2, wherein a [[the]] solvent is used which is selected from dichloromethane, chloroform and dimethylformamide[[,]] and the base, where necessary is, is triethylamine or diisopropylethylamine.

- 4. (Currently Amended): A method according to claim 3 wherein the selective acylation of the primary amino functions of <u>the</u> polyamine[[s]] is carried out with any other activated carboxylic acid derivative known to acylate selectively primary amino functions in the presence of secondary <u>amino functions</u> ones.
- 5. (Currently Amended): A method according to claim 2 wherein the selective mono- or bis-acylation of the primary amino functions of the polyamine[[s]] takes place indirectly and involves the following steps:
- [[1.]] (i) protection of the secondary amino functions of <u>the</u> polyamine[[s]], bearing the trityl protecting group at <u>their its</u> primary amino functions, with the 9-fluorenylmethoxycarbonyl or the trifluoroacetyl group;
 - [[2]] (ii) detritylation;
 - [[3]] (iii) mono- or bis-acylation with the compound[[s]] of step a) of claim 2[[;]]
- [[4]] (iv) complete deprotection and purification, if necessary, by flash column chromatography.
- 6. (Currently Amended): A method according to claim 2 wherein the selective acylation of the secondary amino functions of <u>the</u> polyamine[[s]] involves the following steps:
 - (i) selective trifluoroacetylation of the primary amino functions of the polyamine[[s]];
 - (ii) acylation of the secondary amino functions with the acidic retinoids in the presence of [[the]] a coupling agent PyBroP;
 - (iii) removal of the trifluoroacetyl groups by alkaline hydrolysis.

Appl. No. 10/549,905

Atty. Docket No.: 13907-02

Response to May 12, 2008 Final Office Action

7. (Currently Amended): A pharmaceutical preparation or product containing the <u>one or more conjugate compounds</u> claimed in claim 1 for therapeutical applications in humans.

- 8. (New) A method according to claim 3, wherein a base is used which is triethylamine or diisopropylethylamine.
- 9. (New) A method according to claim 5, which further involves the following step: : (iv) complete deprotection and purification by flash column chromatography.